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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,143	10/21/2003	Kirk J. Hogan	960296.00130	6044

27114 7590 05/20/2005

QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE, SUITE 2040
MILWAUKEE, WI 53202-4497

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,143	HOGAN ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0.0.

DETAILED ACTION

Specification

1. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

For example, page 15, contains a hyperlink.

Priority

2. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a *** of Application No. ***, filed ***, now Patent No. ***." should be entered following the title of the invention or as the first sentence of the specification. Here the current status of all nonprovisional parent applications referenced is not included.

Appropriate correction is required.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of determining whether a canine is susceptible to canine malignant hyperthermia by determining whether a canine nucleic acid sample contains a T1640C mutation or by detecting a nucleic acid encoding SEQ ID NO: 1.

The specification teaches that the presence of heterozygote T1640C mutation is indicative of canine malignant hyperthermia. The specification illustrates the amino acid sequence of exon 15 in dog and four other species. It is noted that the nucleic acid encoding this sequence has not been described nor provided. Figure 3 illustrates the canine amino acid sequence for the normal and variant sequence (beginning with amino acid 527, wherein mutation is at amino acid 547). The specification, page 6, states that "T1640C mutation we mean an alanine to valine change at amino acid 547 in the RYR1 protein. For information regarding the RYR1 region, one of skill in the art may consult reference 23, Priat, 1998 (incorporated by reference)." Upon review of the Priat article, no nucleic acid sequence has been provided for the RYR1 canine nucleic acid. No position 1640 has been described. The specification teaches the nucleotide sequences

of canine regions I and II have been submitted to Genbank (accession #A302128 and #AF302129, respectively). It is noted that accession #A302128 does not exist in Genbank. While AF302128 appears in Genbank, no new matter may be introduced following the filing of the application. Furthermore, even in the event that the specification had properly identified the Genbank Accession Number and the Genbank entry had been available prior to the filing date, the specification does not contain any specific incorporation by reference statement which would allow such material to be incorporated into the instant specification without new matter (MPEP 608.01(p)). Moreover, the specification teaches that the 1640 mutation is located within Region 1 (extends from nucleotides 22-1982, corresponding to amino acids 7-660)(page 19, para 43). The specification also teaches that the MH-associated V547A mutation is in Region II, exon 15 (page 29, Table 3 heading). Therefore, it is unclear where within the undisclosed and uncharacterized region I and II the mutation occurs. Moreover, the specification teaches that the T1640C mutation creates a recognition site for restriction enzyme MscI which generates fragments of 487 bp in length for homozygous and 268 and 219 fragments for heterozygotes (page 20). This information does not provide a clear description of the subject matter because the original region amplified prior to analysis has not been described.

The art does not provide description of any RYR1 canine nucleic acid sequence prior to the filing date of the application. The post filing date are provides a canis familiaris skeletal muscle ryanodine receptor (RYR1) mRNA partial cds (AF302128, October 2001). The nucleic acid provided in the post filing date art can not be relied

upon to describe and enable the instant application. As provided in MPEP 2163, "The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed (see, e.g., Wang Labs. v. Toshiba Corp., 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993)) and should include a determination of the field of the invention and the level of skill and knowledge in the art." Therefore, at the time the invention was made, the RYR1 canine gene had not been described nor had the position of a T1640C mutation been described for the artisan to understand the subject matter material.

The art teaches that numerous mutations in human RYR1 and porcine RYR1 genes are associated with malignant hyperthermia. The art teaches point mutations within each of these known genes which are indicative of susceptibility of the disease.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Specifically, with respect to Claim 1, the specification fails to provide any clear framework that the skilled artisan would be able to use to determine where the T1640C

mutation was located, the flanking sequences such that primers may be designed, or other information which would allow the detection of the single nucleotide change in the undefined gene. The description provided in the specification does not clearly describe with reasonable clarity the invention. Applicant has only describe a single point mutation located at 1640 of an undisclosed, undescribed sequence as being important to canine malignant hyperthermia. Given such a teaching, theoretically, any sequence, regardless of the surrounding sequences which contained a C or T at position 1640 would satisfy the claim. As written, Claim 1 does not require any gene, just position 1640 T-C mutation. Even in the event that the claim were amended to recite canine RYR1 gene, the specification has not described nor disclosed a canine RYR1 gene such that the claim would meet the description guidelines.

As specifically required by Claim 6, a portion of the canine RYR1 gene is amplified. The specification has not provided any indication of how to amplify this region since the specification has not provided the flanking regions which would allow a skilled artisan to design routine primers to the region. The canine RYR1 gene has not been described in the instant specification, nor provided in the art at the time of the invention.

With respect to Claim 7, the instant specification has not taught the skilled artisan how to make the sequence between Exon 14 and 16 of "the RYR1 gene" for the canine species. The specification has not provided a structure for Exon 14 and 16 which would identify the region for the artisan. The artisan would not be reasonably apprised of what

the exons structure is. No nucleic acid sequence has been provided for exon 14 and 16.

With respect to Claim 12, since the specification does not teach the flanking portions of the RYR1 gene, the specification has not described a set of primers useful for amplifying a portion of the canine RYR1 gene. Thus, at the time the invention was made, the specification nor the art taught the canine RYR1 gene. The specification fails to indicate that the sequence. Accordingly, applicant has failed to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention given the lack of the disclosure of the canine gene for RYR1.

With respect to claim 14 directed to primers which comprise SEQ ID NO: 19 and 20, the specification has not described any flanking sequences such that the artisan would be able to design primers which comprise SEQ ID NO: 19 and 20 within the naturally occurring gene.

Claim 15 is directed to a nucleic acid encoding SEQ ID NO: 1. SEQ ID NO: 1 is a partial amino acid sequence from the dog RYR1 gene. The specification and the art fail to teach the canine RYR1 gene prior to the date of filing. The disclosure of a partial amino acid sequence is not representative of a nucleic acid encoding the full gene. A nucleic acid encoding SEQ ID NO: 1 encompasses cDNA, genomic, variants, splice variants, for example which have not been described in the instant specification. From the post filing date art, the full amino acid sequence for the canine RYR1 amino acid is 597 amino acids in length. SEQ ID NO: 1 is 31 amino acids in length. This very short

segment of the protein and the lack of any encoded nucleic acid is not an adequate description of a nucleic acid encoding the RYR1 gene. The full length gene, the full cDNA are each significant embodiments of a nucleic acid encoding SEQ ID NO: 1 which has not been described in the instant specification. Accordingly, applicant has failed to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention given the lack of the disclosure of the canine gene for RYR1. Applicant may wish to consider amending "a nucleic acid encoding SEQ ID NO: 1" to "a nucleic acid encoding an amino acid consisting of SEQ ID NO: 1."

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of determining whether a canine is susceptible to canine malignant hyperthermia by determining whether a canine nucleic acid sample contains a T1640C mutation.

The specification teaches that the presence of heterozygote T1640C mutation is indicative of canine malignant hyperthermia. The specification illustrates the amino acid sequence of exon 15 in dog and four other species. It is noted that the nucleic acid encoding this sequence has not been described nor provided. Figure 3 illustrates the canine amino acid sequence for the normal and variant sequence (beginning with amino acid 527, wherein mutation is at amino acid 547). The specification, page 6, states that "T1640C mutation we mean an alanine to valine change at amino acid 547 in the RYR1 protein. For information regarding the RYR1 region, one of skill in the art may consult reference 23, Priat, 1998 (incorporated by reference)." Upon review of the Priat article, no nucleic acid sequence has been provided for the RYR1 canine nucleic acid. No position 1640 has been described. The specification teaches the nucleotide sequences of canine regions I and II have been submitted to Genbank (accession #A302128 and #AF302129, respectively). It is noted that accession #A302128 does not exist in Genbank. While AF302128 appears in Genbank, no new matter may be introduced following the filing of the application. Furthermore, even in the event that the specification had properly identified the Genbank Accession Number and the Genbank entry had been available prior to the filing date, the specification does not contain any specific incorporation by reference statement which would allow such material to be incorporated into the instant specification without new matter (MPEP 608.01(p)). Moreover, the specification teaches that the 1640 mutation is located within Region 1 (extends from nucleotides 22-1982, corresponding to amino acids 7-660)(page 19, para 43). The specification also teaches that the MH-associated V547A mutation is in

Region II, exon 15 (page 29, Table 3 heading). Therefore, it is unclear where within the undisclosed and uncharacterized region I and II the mutation occurs. Moreover, the specification teaches that the T1640C mutation creates a recognition site for restriction enzyme MscI which generates fragments of 487 bp in length for homozygous and 268 and 219 fragments for heterozygotes (page 20). This information does not provide a clear description of the subject matter because the original region amplified prior to analysis has not been described.

The art does not provide description of any RYR1 canine nucleic acid sequence prior to the filing date of the application. The post filing date are provides a canis familiaris skeletal muscle ryanodine receptor (RYR1) mRNA partial cds (AF302128, October 2001). The nucleic acid provided in the post filing date art can not be relied upon to describe and enable the instant application. As provided in MPEP 2163, "The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed (see, e.g., Wang Labs. v. Toshiba Corp., 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993)) and should include a determination of the field of the invention and the level of skill and knowledge in the art." Therefore, at the time the invention was made, the RYR1 canine gene had not been described nor had the position of a T1640C mutation been described for the artisan to understand the subject matter material.

The art teaches that numerous mutations in human RYR1 and porcine RYR1 genes are associated with malignant hyperthermia. The art teaches point mutations within each of these known genes which are indicative of susceptibility of the disease.

Based upon the teachings in the art at the time the invention was made and in the specification the skilled artisan would not know how to make and use the claimed invention. Specifically, with respect to Claim 1, the specification fails to provide any clear framework that the skilled artisan would be able to use to determine where the T1640C mutation was located, the flanking sequences such that primers may be designed, or other information which would allow the detection of the single nucleotide change in the undefined gene. The skilled artisan would be required to have determined the nucleic acid sequence of the claimed gene, identified the location within the identified nucleic acid before being able to make and use the claimed invention. Determining the nucleotide present at position 1640 within an undisclosed, undescribed nucleic acid, would require undue experimentation. Furthermore, it is unpredictable whether the skilled artisan would obtain the same nucleic acid such that the numbering system would be equivalent.

As specifically required by Claim 6, a portion of the canine RYR1 gene is amplified. The specification has not provided any indication of how to amplify this region since the specification has not provided the flanking regions which would allow a skilled artisan to design routine primers to the region.

With respect to Claim 7, the instant specification has not taught the skilled artisan how to make the sequence between Exon 14 and 16 of "the RYR1 gene" for the canine

species. The skilled artisan would be required to perform undue and unpredictable experimentation to obtain the sequence between exon 14 and 16 of the canine RYR1 gene.

With respect to Claim 12, since the specification does not teach the flanking portions of the RYR1 gene, the skilled artisan would be required to perform undue experimentation to determine RYR1 canine gene specific primers which would amplify nucleotide 1640. Moreover, Claim 14 is directed to primers comprising SEQ ID NO: 19 and 20, however, the skilled artisan would be unclear as to how to modify these primers such that the would still amplify the canine gene.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-11 are indefinite over the recitation "presence of absence of a T1640C mutation". It is unclear what position 1640 is relative to. The specification does not teach a nucleic acid sequence containing over 1640 nucleic acids.

B) Claim 6 is indefinite because it is unclear what "the canine RYR1 gene" encompasses. The specification does not teach a nucleic acid sequence for the canine

RYR1 gene and the prior art does not teach a nucleic acid sequence for the canine RYR1 gene.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-6 of U.S. Patent No. 6,664,059.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentable distinct from each other because Claims 1-15 of the instant application is generic to all that is

recited in Claims 1-6 of U.S. Patent No. 6,664,059. That is, Claims 1-6 of 6,664,059 falls entirely within the scope of Claims 1-15, or in other words, Claims 1-15 are anticipated by Claims 1-6 of 6,664,059. Here, claims 1-5 of U.S. Patent No. 6,664,059 recites a method determining whether a canine is susceptible to canine malignant hyperthermia by amplifying using SEQ ID NO: 19 and 20, digesting with an enzyme and detecting. In the instant application, Claim 1 and Claim 15 are generically drawn to methods of detecting the mutation of 6,664,059. Additionally, the kit of instant Claim 12-14 is anticipated by the kit of Claim 6. The instant kits are generic to Claim 6 of 6,664,059 which requires SEQ ID NO: 19 and 20 and MscI. Therefore, instant Claims 12-14 are anticipated by the patented kit of 6,664,059.

Conclusion

8. No claims allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

JEANINE A. GOLDBERG
PRIMARY EXAMINER

5/17/05